In the Claims

Applicant has submitted a new complete claim set showing marked up claims with insertions indicated by underlining and deletions indicated by strikeouts and/or double bracketing.

Please cancel claims 4, 6, 9-11, 15, 17, 20-22, 24, 25, 27, 29, 30, 35, 37 and 40-51 without prejudice or disclaimer.

1. (Original) A method for diagnosing a disorder associated with altered β-secretase and/or γ-secretase processing of substrates, comprising

measuring the stability of a secretase pathway associated protein in a biological sample from a subject, wherein increased protein stability relative to that in a control biological sample is an indication that the subject has a disorder associated with altered β-secretase and/or γ-secretase processing of substrates.

2. (Original) The method of claim 1, wherein the disorder associated with altered β-secretase and/or γ-secretase processing of substrates is an Aβ-accumulation-associated disorder.

3. (Original) The method of claim 1, wherein the disorder associated with altered β-secretase and/or γ-secretase processing of substrates is selected from the group consisting of cancer, neurological diseases, immunologic diseases and glycoconjugate metabolism disorders.

4. (Canceled)

5. (Original) The method of claim 1, wherein the secretase pathway associated protein is selected from the group consisting of: presenilins, nicastrin/Aph2, BACE, Aph1a, and Pen-2 protein.

6. (Canceled)

7. (Original) The method of claim 1, wherein the subject is human.

8. (Original) The method of claim 1, wherein the subject is at risk of developing Alzheimer's disease.

9-11. (Canceled)

12. (Original) A method for determining onset, progression, or regression, of a disorder associated with altered β-secretase and/or γ-secretase processing of substrates in a subject, comprising:

measuring the stability of a secretase pathway associated protein in a first biological sample of a subject,

measuring the stability of the secretase pathway associated protein in a second biological sample of a subject obtained at a second time,

comparing the measurement of stability in the first sample to the measurement of stability in the second sample as a determination of the onset, progression, or regression of the disorder associated with altered β-secretase and/or γ-secretase processing of substrates.

13. (Original) The method of claim 12, wherein the disorder associated with altered β-secretase and/or γ-secretase processing of substrates is an Aβ-accumulation-associated disorder.

14. (Original) The method of claim 12, wherein the disorder associated with altered β-secretase and/or γ-secretase processing of substrates is selected from the group consisting of cancer, neurological diseases, immunologic diseases and glycoconjugate metabolism disorders.

15. (Canceled)

16. (Original) The method of claim 12, wherein the secretase pathway associated protein is selected from the group consisting of: presenilins, nicastrin/Aph2, BACE, Aph1a, and Pen-2 protein.

17. (Canceled)

18. (Original) The method of claim 12, wherein the subject is human.

19. (Original) The method of claim 12, wherein the subject has been diagnosed with Alzheimer's disease or is at risk of developing Alzheimer's disease.

20-22. (Canceled)

23. (Original) A method for identifying compounds that modulate caspase activation-induced stabilization of a secretase pathway associated protein comprising

contacting cells that have been induced to undergo caspase activation with a candidate modulator of secretase pathway associated protein stabilization, and

measuring the stability of the secretase pathway associated protein, wherein a difference in the stability of the protein relative to the stability of the protein in untreated cells is an indication that the candidate modulator is a compound that modulates the caspase activation-induced stability of the secretase pathway associated protein.

24-25. (Canceled)

26. (Original) The method of claim 23, wherein the secretase pathway associated protein is selected from the group consisting of: presenilins, nicastrin/Aph2, BACE, Aph1a, and Pen-2 protein.

27. (Canceled)

28. (Original) The method of claim 23, wherein the cells are neuronal cells.

29-30. (Canceled)

31. (Original) The method of claim 23, wherein the caspase activation induces apoptosis.

32. (Original) A method for treating or preventing an disorder associated with altered β-secretase and/or γ-secretase processing of substrates, comprising

administering to a subject in need of such treatment an effective amount of a compound that is an inhibitor of the caspase activation-associated stabilization or apoptosis-associated stabilization of a secretase pathway associated protein or secretase pathway associated protein complex.

33. (Original) The method of claim 32, wherein the disorder associated with altered β-secretase and/or γ-secretase processing of substrates is an Aβ-accumulation-associated disorder.

34. (Original) The method of claim 32, wherein the disorder associated with altered β-secretase and/or γ-secretase processing of substrates is selected from the group consisting of cancer, neurological diseases, immunologic diseases and glycoconjugate metabolism disorders.

35. (Canceled)

36. (Original) The method of claim 32, wherein the secretase pathway associated protein is selected from the group consisting of: presenilins, nicastrin/Aph2, BACE, Aph1a, and Pen-2 protein.

37. (Canceled)

38. (Original) The method of claim 32, wherein the subject is a human.

39. (Original) The method of claim 32, wherein the subject has been diagnosed with Alzheimer's disease or is at risk of developing Alzheimer's disease.

40-51. (Canceled)